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- with international search report (Art. 21(3))
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(88) Date of publication of the international search report:

16 October 2014

(54) Title: MODULATION OF APOLIPOPROTEIN C-III (APOCIII) EXPRESSION IN LIPOPROTEIN LIPASE DEFICIENT
(LPLD) POPULATIONS

(57) Abstract: Provided are methods, compounds, and compositions for reducing expression of ApoCIII mRNA and protein for treating, preventing, delaying, or ameliorating Fredrickson Type I dyslipidemia/FCS/LPLD, in a patient. Such methods, compounds, and compositions increase HDL levels and/or improving the ratio of TG to HDL and reducing plasma lipids and plasma glucose in the patient, and are useful to treat, prevent, delay, or ameliorate any one or more of pancreatitis, cardiovascular disease, metabolic disorder, and associated symptoms.



WO 2014/127268 A3

INTERNATIONAL SEARCH REPORT

international application no.

PCT/US 14/16546

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 48/00; C12N 15/11; C07H 21/04 (2014.01)

USPC - 514/44R; 514/44A; 536/24.5, 536/23.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A61K 48/00; C12N 15/11; C07H 21/04 (2014.01)

USPC - 514/44R; 514/44A; 536/24.5, 536/23.5, 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

IPC(8) - A61K 48/00; C12N 15/11; C07H 21/04 (2014.01) - see keyword below

USPC - 514/44R; 514/44A; 536/24.5, 536/23.5, 536/23.1 - see keyword below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST(USPT,PGPB,EPAB,JPAB); PatBase; Medline, Google: Fredrickson Type I dyslipidemia, familial chylomicronemia syndrome, FCS, Lipoprotein Lipase Deficiency, LPLD, apolipoprotein C-III, ApoC-III, antisense, hypertriglyceridemia, triglyceride, TG, gap, cardiovascular, metabolic, pancreatitis, HDL, 5' wing, 3' wing, 2'-O-methoxyethyl, 5'-methy

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011/0060030 A1 (CROOKE et al.) 10 March 2011 (10.03.2011), Abstract, para [0035], [0072], [0078], [0093], [0150], [0201], [0202], [0241], [0246], [0258], SEQ ID NO: 18, and SEQ ID NO: 87	1-9, 21-26
Y	BORGHEI et al. Familial Chylomicronemia Syndrome Presenting Familial Lipoprotein Lipase Deficiency. J. Nepal Paediatr. Soc. 2010, Vol 30(2), p. 110-112. Abstract; pg 110, col 1, para 1; and pg 112, col 2, top para	1-9, 21-26
A	US 2012/0270929 A1 (CROOKE et al.) 25 October 2012 (25.10.2012), para [0116], and [0118]-[0131]	1-9, 21-26
A	BURY et al. Immunonephelometric quantitation of the apolipoprotein C-III in human plasma. Clin Chim Acta. 1985, Vol. 145(3), p. 249-58. Entire documentation, especially Abstract	1-9, 21-26
A	WO 2011/123401 A1 (MEYERS et al.) 06 October 2011 (06.10.2011), pg 2, ln 7-13.	1-9, 21-26



Further documents are listed in the continuation of Box C.



* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 April 2014 (22.04.2014)

Date of mailing of the international search report

18 AUG 2014

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
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INTERNATIONAL SEARCH REPORT

international application no.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

☐

on paper

☒

in electronic form

b. (time)

☒

in the international application as filed

☐

together with the international application in electronic form

☐

subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

international application no.

PCT/US 14/16546

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 10-20, 27-34
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.